REMARKS

Applicants have amended claims 4, 6 and 7 to correct clerical and typographical errors.

Claims 4, 6 and 7 are objected to for containing informalities. Applicants have amended the claims to eliminate the informalities.

Claims 1-4, 6 and 7 stand rejected under 35 U.SC. 112, first paragraph for purportedly being non-enabled. Applicants disagree and in view of the following remarks, Applicants request the Examiner to reconsider and withdraw the rejection.

> If the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that in vitro data did not support in vivo applications).
>
> MPEP 2164.02

For drug trials to be approved for the market, those of skill in the art routinely use animal models (either natural or transgenic) in preclinical stages and extrapolate the results from those models to clinical efficacy in human beings. Such animal models are reliable tools to obtain preclinical data which can be subsequently extrapolated to human beings in clinical stages. Applicants direct the Examiner's attention to the fact that Applicants did not select animal models arbitrarily but rather selected animal models that are accepted by the scientific community. For example Annex 1 (attached) (Sarasa & Pesinin, Curr Alzheimer Research (2009) 6:171-178) deals with several animal species that

develop amyloid deposits in a very similar way as human beings do, thus said species can be used as natural models for assays of new therapies against Alzheimer's disease and other amyloid related diseases.

In addition, using humans at the first stages of the development of a drug just to get clinical results to provide support for a patent application would be unacceptable for obvious ethical reasons. Therefore, most of the drugs currently marketed are protected by patents wherein the efficacy is supported with the result obtained in animal models, or just with *in vitro* data. For instance, one clear example is the active ingredient donepezil, marketed as Aricept™, being its main therapeutic use is in the treatment of Alzheimer's disease. The FDA Orange Book lists the US 5,100,901 as a patent protecting the use for the treatment of Alzheimer using said drug. Said patent has more than 200 synthetic examples but just a simple experiment in an animal model showing the activity in the claimed compound family.

Furthermore, the present application provides a method to decrease levels of Aß peptide in the brain of a subject. The side effects that appear in another method of treatment using other different peptides, is not relevant to the claimed methods and does not render the disclosure of the present invention insufficient. Moreover, the clinical trial described by Solomon, far from denying the enabling disclosure of the instant application, supports the extrapolation made in the application, i.e. from animal model to human beings. The peptides disclosed in Vellas et al. firstly showed activity in the animal models (see *Nature* 400:173-177 (1999) by Schenk, D. et al. or *Nature* 408: 979-982 (2000) by Janus, C. et al), and later this activity was confirmed in the trial performed in human beings. Years after the trial that the Examiner cited took place it was demonstrated that the patients inoculated by the peptide showed a decrease in the advance of the disease (see Annex 3, Vellas et al. Curr. Alzheimer Res. (200() 6:144-151). This result corroborates the vaccination properties shown by the peptides in the animal model. In short, the fact that a specific peptide may produce to side

effects in some patients does not deny the fact that the peptide really works *in vivo*.

Finally, the Examiner states that the claims are not limited to a maximum number of residues that may be eliminated from SEQ ID NO:2 and SEQ ID NO:3 N- or C-terminal ends, and thus claim a peptide that may be too short to obtain a immune response that is specific and effective. However, one of skill in the art interpreting the claims within the context of the invention and appreciating that the sequences must retain good activity could find active variants by modifying the length of SEQ ID NO:2 and SEQ ID NO:3, without resorting to undue experimentation.

In view of the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 112, first paragraph.

Claims 1-4, 6 and 7 stand rejected under 35 U.S.C. 102(b) for purportedly being anticipated by WO 00/72880 A2 (Schenk et al.) and stand rejected under 35 U.SC 102(e) for purportedly being anticipated by US 2006/0188512 (Yednock et al.). Applicants disagree and in view of the following remarks request that the Examiner reconsider and withdraw the rejection.

> Anticipation under 35 U.S.C. §102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention.
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> *Electro Med. Sys. S.A. v. Cooper Life Sciences*, 32 USPQ2d 1017, 1019 (Fed. Cir. 1994).

The Examiner states that Schenk and Yednock disclose a method of treating a disease associated with amyloid deposits, such as Alzheimer's disease, which comprises administering an effective amount of Aß peptide to provoke an immunogenic response against said Aß epitopes. However, the fragments

selected by Schenk are those from the N-terminal domain and thus Shenk teaches away from Applicants' invention as claimed.

For example Schenk clearly states that "*fragments from the N-terminal half of Aβ are preferred*" (page 14, line 32 and page 15, lines 1-4), specially fragments from residues 1 to 11 of Aß. In fact, animals that received Aß33-42 (SEQ ID 3) conjugate pBx6 or PBS had no Aß-stimulated response (page 67, lines 7-8), as table 5 shows. Thus, Schenk et al. does to teach that an immunogen comprising peptide SEQ ID NO: 3 or any other fragment from the C-terminal region would provide a therapeutic effect by reducing beta-amyloid plaques. In contrast, the present application and the additional result obtained by the inventors, filed herewith as Annex 2, clearly demonstrates that SEQ ID NO:3 is capable of inhibiting both aggregation of ß-amyloid peptides and the disaggregation of the already aggregated peptide.

Likewise, Yednock states that "*fragment Aβ15-24 and subfragments of 7-9 contiguous aminoacids thereof are preferred*" (paragraph [0034]). The provided experimental data are directed to immunization with N-terminal fragments (Aß1-5, Aß3-9 and Aß5-11) and central fragment (Aß-15-24). Thus Yednock also teaches away from the present invention.

As SEQ ID NO:2 is a shortening of SEQ ID NO:3 Shenk and Yednock also teach away for methods that use a peptide comprising SEQ ID NO: 2.

Use of SEQ ID NO:2 is not a random selection among the Aß fragments, but a purposeful selection, in the sense that it possesses the ability of decreasing levels of Aß peptide in a exceptional way, as the application as filed and the enclosed further experimental results show, contrary to the expectations in the art.

Therefore, Schenk and Yednock fail to teach the ability of SEQ ID NO:3 or SEQ ID NO: 2 to reduce the accumulation of amyloid peptide and as such the

use of these sequences as immunogens is not anticipated by either Schenk or Yednock.

The foregoing remarks make clear that that claimed methods are not anticipated by Schenk or Yednock and Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 102(b) in view of Schenk et al. and under 102(e) in view of Yednock et al.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323, Docket No. 105090.61194US.

Respectfully submitted,

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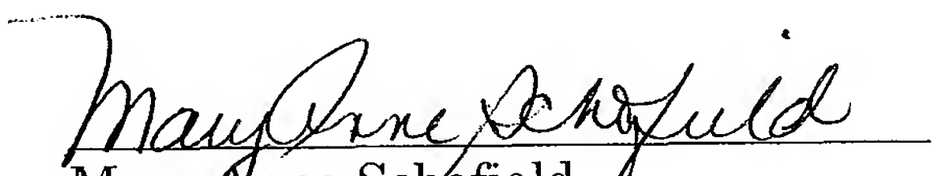

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